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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,976	09/02/1999	Tahtinen et al	227-135	6995

7590 07/18/2002

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EXAMINER	
SALIMI, ALI REZA	
ART UNIT	PAPER NUMBER
1648	7

DATE MAILED: 07/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/622,976	Tahtinen et al
Examiner	**Art Unit**
A. R. SALMI	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *2 1/2*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence letter*

DETAILED ACTION

Claims 1-15 are pending.

Submitted Information Disclosure Statement (I.D.S) is noted.

Notice of draftsperson's patent drawing review (PTO 948) is enclosed.

Response to Amendment

The receipt of preliminary amendment of 8/25/2000, is acknowledged.

Sequence Requirements

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, foe instance see page 11 of the specification.

Full compliance with the sequence rules is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite, the intended papillomavirus is not defined. Moreover, claims 1, and 8 are indefinite since the intended metes and bounds of parts "(ii)" and "(iii)" of the said claims are not defined. This affects the dependent claims.

In addition, claims 1, 7, 8, 12, 13 are vague and indefinite for recitation of "immunologically active fragment thereof", the intended fragment(s) is/are not defined. Is two amino acids intended? The claims have been interpreted in light of the specification and since the specification does not provide the metes and bounds of the intended fragments the claim is considered to be indefinite. Moreover, the limitation of "active" is a relative terminology. This affects the dependent claims.

Claim 5 is confusing for recitation of "I" in line 2, appropriate correction is requested.

Claim 6 is indefinite for recitation of "comprising", there has to be more than one element in a composition, but only one is present. Is a carrier intended? This affects the dependent claim 7.

Claim 10 provides for the use of self-replicating vector, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 10 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 11 provides for the use of manufacture of a vaccine, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 11 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex*

parte Dunki, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 12 is indefinite for recitation of "effective amount", the amount is not provided. The claim has been interpreted in light of the specification and since the specification does not provide the metes and bounds of the "effective amount" the claim is considered to be indefinite.

Claim Rejections - 35 USC § 112

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for induction of **immune response only** by utilizing a vector comprising recombinant bovine papillomavirus vector E1, E2 genes, minimal origin of replication of bovine papillomavirus (MO), a bovine papillomavirus microchormosomal maintenance element (MME) being able to express entire NEF, or entire REV, or entire TAT singularly, does not reasonably provide enablement for (1) vaccine for DNA immunization against HIV, (2) against combination vaccine or combination immune response against TAT, NEF, or REV, (3) utilization of any and all papillomavirus types E1, E2 genes, MO, MME regions, (4) method of preventing HIV by administering effective amount, (5) fragment thereof of either NEF, TAT, or NEF. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The specification lacks proper teaching within the broad scope of claimed invention. At the outset applicants are reminded that this filed is highly unpredictable and the teaching of the

specification should provide adequate teaching to one ordinary skill in the art to practice the invention absent undue experimentation. **First**, there are no challenge study present in the specification to merit the limitation of vaccine against HIV. Induction of immune response is not sufficient showing of protection against a deadly virus like HIV. A challenge study in an appropriate model where the exact infection or disease can be replicated is needed to show whether or not full protection can be achieved when a full dose of virus is injected. The specification does not show this and undue experimentation would be required to establish such a fact. In addition, as evidence see post filing state of the art which teaches that DNA vaccine against HIV is not capable of inducing protective response (see abstract in Barouch et al, Intervirology, 2000, Vol. 43, pages 282-287).

Second, the state of art teaches that combination of early genes of HIV do indeed interfere with efficacy of one another and should be administered in a single form, as evidence see post filing teaching by Kjerrstrom et al, where they teach that "co-immunization" with Tat, NEF, and REV result in inhibition of immune response (Kjerrstrom et al, Virology, 2001, Vol. 284, pages 46-61, especially see abstract, and pages 46- 47, bridging paragraph). Hence, the proper utilization of composition or method of mixture vectors absent adequate teaching would require absent undue experimentation.

Third, the specification does not teach or consider whether or not adverse anti vector response should be considered. The invention is directed to self-replication vector which comprises all types of papillomavirus genes and regulatory regions. There is great possibility that a massive

immune response can be forged against the papillomavirus E1 and E2 genes and not necessarily against NEF, TAT, or NEF. In addition, there is no teaching what the immune response would be like once human papillomavirus E1, E2, human minimal origin of replication of papillomavirus (MO), and human papillomavirus microchormosomal maintenance element (MME) are employed as part of self replicating vector. What if the patient is already infected with human papillomavirus, is the immune response going to be the same? Is the administration of vector having human papillomavirus going to raise antibodies against human papillomavirus or the HIV early genes? Still, the vector might trans-complement if the patient is infected with papillomavirus and a full blown papilloma infection would ensue, shouldn't this be considered? Thus, absent adequate teaching undue experimentation would be required.

Fourth, the specification lacks teaching with regard to composition or method of preventing HIV. The patient infected with HIV for the most part are immunocompromized, and there is no teaching how HIV maybe prevented. Induction of immune response in a model that the natural infection can not be replicated in, is not the same as preventing the disease. In addition, the specification does not set forth any guidance for "effective amount" that would help in preventing the infection. No challenge study is present to warrant prevention limitation.

Fifth, there is no teaching or guidance provided about any fragments of NEF, TAT, or NEF capable of inducing any types of immune response, absent teaching undue experimentation would be required.

In conclusion, Applicants have general statements regarding the vaccine composition, prevention of HIV, mixture vectors, and utilization of any and all papillomaviruses regions in a self replicating vector, as stated above. However with regard to an unpredictable field, this does not constitute an adequate disclosure. See Fiers v. Revel (25USPQ2d 1601 at 1606; and also decision by the Federal Circuit with regard to the enablement issues see Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1001-1007). For example, the CAFC stated that "It is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute enablement." (See page 1005 of the decision). This means that the disclosure must adequately guide the art worker to determine, without undue experimentation. The applicant can not rely on the knowledge of those skilled in the art to enable the claims without providing adequate teaching. Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claim. Many of these factors have been summarized *In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).*

Claim Rejections - 35 USC § 112

It appears from reading the specification that for a successful practice of claims, 1, 4, 5 the pBNtKREV, pBNsr∝TAT or pBNsr∝NEF is an essential element. The specification does not provide a reproducible method to make the specific vectors now claimed. Hence, It would require an undue experimentation to enable the invention. Therefore, deposits of vectors are

required. The specification does not give the exact boundaries of various genes, hence, one skilled in the art could not reproduce exactly the structure of the named isolate.

For the reasons discussed above, it is apparent that the vectors specifically recited in the claims are required to practice the claimed invention. As a required element they must be known and readily available to the public or obtainable by repeatable method set forth in the specification, or otherwise readily available to the public. If not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by deposits of the recited vectors See 37 CFR 1.802.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the following criteria have been met:

(a) during the pendency of this application, access to the deposits will be afforded to one determined by the commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

© the deposits will be maintained in the public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d)a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposits will be replaced if they should become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-37 CFR 1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ustav (WO 97/24451), and Hinkula et al (Journal of Virology, July 1997).

The claims are directed to self-replicating vector comprising E1, E2 papillomavirus genes as well as minimal origin of replication of papillomavirus (MO), a papillomavirus microchormosomal maintenance element (MME) being able to express NEF, or REV, or TAT of human immunodeficiency virus. In addition, the claims are directed to method or generating the vectors and method of treating HIV.

Ustav (WO 97/24451) taught the self-replicating vector comprising E1, E2 genes, minimal origin of replication of papillomavirus (MO), a papillomavirus microchormosomal maintenance element (MME) being able to express heterologous genes (see the claims). In addition, Ustav taught methods of producing the vector (see the abstract, and claims 1-3). Furthermore, the above cited patent taught which heterologous genes can be utilized within the vector including HIV antigens (see page 34, lines 13-17). The only difference between the cited world patent and

the claimed invention is that Ustav does not specifically recite NEF, REV, or TAT as antigens to be inserted into vector.

Hinkula et al taught DNA immunization of plasmid wherein each plasmid comprised TAT, NEF, or NEV or HIV (see the abstract, and Table 3). In addition, they clearly taught that plasmid DNA carrying any of three HIV genes of NEF, REV, TAT induced immune response in mice (see bridging paragraph of page 5535-5536). This differs form the claims since the reference does not teach the self-replicating vector having E1, E2 genes, minimal origin of replication of papillomavirus (MO), a papillomavirus microchormosomal maintenance element (MME).

Hence, one of ordinary skilled in the art at the time of filing would have been highly motivated to combine the teaching of Ustav and Hinkula et al to induce immune response against TAT, NEF, or REV absent unexpected results. The prior art taught the self-replicating vector, as taught by Ustav, and the prior art also taught the antigens as well taught that DNA immunization induces immune response against NEF, TAT, or REV. One of skill in the art being familiar with the state of the art as cited above would not have anticipated any unexpected results by combining the teaching of above cited art, as no unexpected results have been reported. Therefore, the invention as a whole is considered to be prima facie obvious absent unexpected results.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woo et al (WO 94/12629), and Hinkula et al (Journal of Virology, July 1997).

The claims are directed to self-replicating vector comprising E1, E2 papillomavirus genes as well as minimal origin of replication of papillomavirus (MO), a papillomavirus microchormosomal maintenance element (MME) being able to express NEF, or REV, or TAT of human immunodeficiency virus. In addition, the claims are directed to method or generating the vectors and method of treating HIV.

Woo et al (WO 94/12629) taught the self-replicating vector comprising E1, E2 genes, minimal origin of replication of papillomavirus (MO), a papillomavirus microchormosomal maintenance element (MME) being able to express heterologous genes (see the claims). In addition, Woo et al taught which heterologous genes can be utilized within the vector antigens (see claim 30). The only difference between the cited world patent and the claimed invention is that Woo et al did not specifically recite NEF, REV, or TAT as antigens to be inserted into vector.

Hinkula et al taught DNA immunization of plasmid wherein each plasmid comprised TAT, NEF, or NEV or HIV (see the abstract, and Table 3). In addition, they clearly taught that plasmid DNA carrying any of three HIV genes of NEF, REV, TAT induced immune response in mice (see bridging paragraph of page 5535-5536). This differs form the claims since the reference does not teach the self-replicating vector having E1, E2 genes, minimal origin of replication of papillomavirus (MO), a papillomavirus microchormosomal maintenance element (MME).

Thus, one of ordinary skilled in the art at the time of filing would have been highly motivated to combine the teaching of Woo et al and Hinkula et al to induce immune response against TAT, NEF, or REV of HIV absent unexpected results. The prior art taught the self-replicating vector, as taught by Woo et al, and the prior art also taught the antigens as well taught that DNA immunization induces immune response against NEF, TAT, or REV. One of skill in the art being familiar with the state of the art as cited above would not have anticipated any unexpected results by combining the teaching of above cited art, as no unexpected results have been reported. Therefore, the invention as a whole is considered to be prima facie obvious absent unexpected results.

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to A. R. Salimi whose telephone number is (703) 305-7136. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-3014, or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

A. R. Salimi

7/17/2002

ALI R. SALIMI
PRIMARY EXAMINER

Application No.: 09/823,476

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s)

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE